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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/600,493	07/18/2000	Jack Wands	MGH-0026	3498

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EXAMINER	
LIETO, LOUIS D	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 11/30/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action Before the Filing of an Appeal Brief	**Application No.** 09/600,493	**Applicant(s)** WANDS ET AL.	
	Examiner Louis D. Lieto	**Art Unit** 1632	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 27 October 2005 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: *None*.
   Claim(s) objected to: *None*.
   Claim(s) rejected: *4, 6-8,17,20-28& 48*.
   Claim(s) withdrawn from consideration: *None*.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
12. ☒ Note the attached Information Disclosure Statement(s). (PTO/SB/08 or PTO-1449) Paper No(s). 10/27/05
13. ☐ Other: _____.

Anne-Marie Falk

ANNE-MARIE FALK, PH.D
PRIMARY EXAMINER

Continuation of 13. Other: The objection to claim 48 as being dependent upon a cancelled base claim is withdrawn in view of applicant's amendment to the claim.

The rejection of claims 4, 6, 7, 8, 17, 20-28 and 48 under 35 U.S.C. 112, first paragraph is maintained, because the specification, while being enabling for a recombinant nucleic acid molecule consisting of a nucleotide sequence encoding hepatitis C virus nonstructural proteins NS3, NS4 and NS5, wherein said nucleotide sequence is operably linked to regulatory elements, said regulatory elements comprising a promoter, enhancer, polyadenylation sequence, and at most the 9 most 3' nucleotides of the 5'UTR of a hepatitis C virus, and a method of inducing an immune response by administration of said recombinant nucleic acid molecule, does not reasonably provide enablement for a recombinant nucleic acid molecule consisting of a nucleotide sequence encoding hepatitis C virus nonstructural proteins NS3, NS4 and NS5, wherein said nucleotide sequence is operably linked to regulatory elements, said regulatory elements comprising a promoter, enhancer, polyadenylation sequence, and a 5' untranslated region from any gene The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Applicant argues that the specification provides enablement for a construct encoding the NS3, NS4 and NS5 HCV proteins operably linked to regulatory elements, comprising, among others a HCV-5'UTR of any length. Further applicant points out that the specification states that the 5'UTR can include the last 9, 50, 100, 150, 200, 250, 300, or all of the HCV 5' UTR nucleotides. However, the specification does not point out what effect these 50 nucleotide increments have on expression of the construct. As previously stated in the office action of 7/28/05, applicant supplied reference of Tokushige et al. indicates that it is disadvantageous to include the entire 5'UTR of HCV in an expression vector designed to induce an immune response. Further, Yoo et al. states that "(1) the full-length 5' UTR of HCV-1 RNA is translationally inactive...[and] (2) an efficient cis-acting element which represses translation is found at the 5' terminus." {Yoo et al. (1992) Virology 191:889-899; Abstract}. Based on the disclosure of Yoo et al. the skilled practitioner would not predict that a construct containing the 5' UTR region of HCV would produce sufficient protein to produce a protective immune response in a mammal. Finally, in the instant case, there is no evidence in the specification which supports that any length fragment of the 5'UTR of HCV could be used in the claimed construct and produce sufficient protein to produce a protective immune response in a mammal.

Applicant argues that the guidance of Yoo et al. on the PEST-IV element would allow a skilled practitioner to predict that a construct containing regions of the 5'UTR, such as the PEST-IV element would produce increased levels of HCV NS3, NS4, or NS5 proteins in comparison to a construct lacking the 5'UTR, and thus increases the likelihood of producing a protective immune response in a mammal. First, it is noted that it is not apparent that the guidance of Yoo et al. was incorporated by reference into the specification. Second, mere reference to another application, patent, or publication is not an incorporation of anything therein into the application containing such reference for the purpose of the disclosure required by 35 U.S.C. 112, first paragraph. In re de Seversky , 474 F.2d 671, 177 USPQ 144, (CCPA 1973). In addition to other requirements for an application, the referencing application should include an identification of the referenced patent, application, or publication. Particular attention should be directed to specific portions of the referenced document where the subject matter being incorporated may be found. MPEP 608.01(p). In the instant case applicant is arguing that one of skill in the art would know based on the reference of Yoo et al. that the PEST-IV element should be included in the 5'UTR in order to increase expression of the NS3, NS4 and NS5 proteins, and negative elements should be eliminated. Figure 1 of Yoo et al. indicates that the full length HCV 5'UTR produces undetectable amounts of the CAT protein. Applicant's arguments indicate that the PEST-IV element is critical to practice the claimed invention, however there are no teachings in the specification on the required presence of the PEST-IV element in the HCV 5'UTR of the construct, and/or the exclusion of any negative elements in either the specification or the claims as currently filed. Finally, it is noted that applicant's claims are not limited to a 5'UTR from HCV-1, which is the one disclosed by Yoo et al. (pg. 895, Discussion). Yoo et al. teaches that the HCV-1 5'UTR lacks a IRES site, while 5'UTRs of HCVs from group II and III contain IRES sites (pg. 895, Discussion). Further, Yoo et al. teaches that the nucleotides sequences of 5'UTRs of different HCV groups differ by 3 to 6% (pg. 895-896, Discussion). . Therefore, given the lack of guidance in the specification on the requirement of the presence of a the PEST-IV element in the HCV 5'UTR of the claimed construct , and the lack of guidance in the specification on the sequence differences of various 5'UTRs from different HCV groups and how this affects expression levels the skilled practitioner would be unable to predict how to practice the claimed invention, except as a recombinant nucleic acid molecule consisting of a nucleotide sequence encoding hepatitis C virus nonstructural proteins NS3, NS4 and NS5, wherein said nucleotide sequence is operably linked to regulatory elements, said regulatory elements comprising a promoter, enhancer, polyadenylation sequence, and at most the 9 most 3' nucleotides of the 5'UTR of a hepatitis C virus, and a method of inducing an immune response by administration of said recombinant nucleic acid molecule, without undue and extensive experimentation.